

Practitioner's Docket No. 701586-052823-US

PATENT

IN THE UNITED STATES RECEIVING OFFICE

| International Application Number | International Filing Date | International Earliest Priority Date |
|-------------------------------------|-----------------------------------|---|
| PCT/US2003/30701 | 30 September 2003 (30.09.2003) | 30 September 2002 (30.09.2002) |

TITLE OF INVENTION: METHODS OF TREATING CANCER USING ADENOSINE AND ITS ANALOGS

APPLICANT(S) FOR EO/DO: The Trustees of Boston University
INVENTOR(S)/APPLICANT(S) FOR US: RAVID, Katya and LU, Jun

CERTIFICATE OF MAILING

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Date: June 21, 2005

Debra J. Kellom
 Debra J. Kellom

MAIL STOP PCT
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir/Madam:

INFORMATION DISCLOSURE STATEMENT

In accordance with the provisions of 37 C.F.R. §1.56, 1.97, and 1.98, Applicants wish to bring to the Examiner's attention the following references, References C1-C48, cited in the attached Forms PTO/SB/08a and b.

REMARKS

In accordance with the provisions of 37 C.F.R. §1.97, this statement is being filed:

- X (1) within three (3) months of the Filing Date or before the mailing date of the First Office Action on the merits; or

- ____ (2) within three months of the mailing date of the PCT International Search Report;
or
- ____ (3) after the period defined in (1) but before the mailing date of a **Final Rejection** or **Notice of Allowance**, and the requisite Certification or fee under Rule 1.17(p), namely **\$180.00**, is included herein; or
- ____ (4) after the mailing date of a **Final Rejection** or **Notice of Allowance** but before the payment of the **Issue Fee**, and the requisite Certification, petition, and petition fee are included herein.

____ A copy of the International Search Report is enclosed herewith.

It is respectfully requested that each of the documents shown on the attached form(s) PTO/SB/08a be made of record in this application.

Copies of these documents (CHECK ONE):

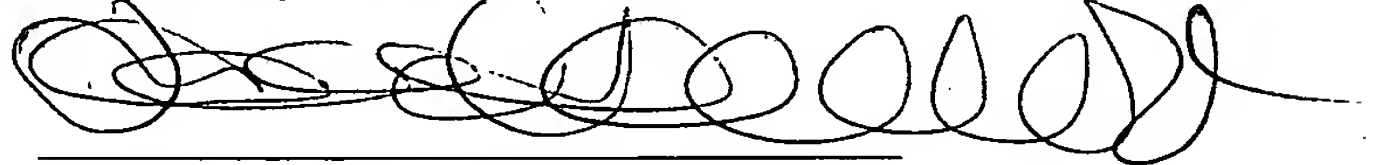
- X are enclosed herewith that have not been previously submitted; or
- ____ have been cited in the parent application, and are thus not being resubmitted herein.

FEE AUTHORIZATION

The Commissioner is authorized to charge fee deficiencies or credit overpayments associated with this submission to the NIXON PEABODY LLP Deposit Account No. 50-0850.

Date: June 21, 2005

Respectfully submitted,



Ronald I. Eisenstein (Reg. No. 30,628)
Leena H. Karttunen (L0207)
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| | | | | Application Number | 10/529,524 |
| | | | | Filing Date | 03/29/2005 |
| | | | | First Named Inventor | Katya Ravid |
| | | | | Art Unit | To be assigned |
| | | | | Examiner Name | To be assigned |
| Sheet | 1 | of | 6 | Attorney Docket Number | 701586-052823-US |

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| Sheet | 2 | of | 6 | Attorney Docket Number | 701586-052823-US |

| NON PATENT LITERATURE DOCUMENTS | | | | |
|---------------------------------|-----------------------|---|----------------|--|
| Examiner Initials* | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published | T ² | |
| | C1 | Altucci, L., Addeo, R., Cicatiello, L., Dauvois, S., Parker, M. G., Truss, M., Beato, M., Sica, V., Bresciani, F., and Weisz, A. 17beta-Estradiol induces cyclin D1 gene transcription, p36D1-p34cdk4 complex activation and p105Rb phosphorylation during mitogenic stimulation of G(1)-arrested human breast cancer cells. <i>Oncogene</i> , 12: 2315-2324, 1996. | | |
| | C2 | Barbieri, D., Abbracchio, M. P., Salvioli, S., Monti, D., Cossarizza, A., Ceruti, S., Brambilla, R., Cattabeni, F., Jacobson, K. A., and Franceschi, C. Apoptosis by 2-chloro-2'-deoxy-adenosine and 2-chloro-adenosine in human peripheral blood mononuclear cells. <i>Neurochem Int</i> , 32: 493-504, 1998. | | |
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| | C5 | Cataldo, L. M., Zhang, Y., Lu, J., and Ravid, K. Rat NAP1: cDNA cloning and upregulation by Mpl ligand. <i>Gene</i> , 226: 355-364., 1999. | | |
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| | C9 | Dubik, D. and Shiu, R. P. Mechanism of estrogen activation of c-myc oncogene expression. <i>Oncogene</i> , 7: 1587-1594, 1992. | | |

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| | | | | Art Unit | To be assigned |
| | | | | Examiner Name | To be assigned |
| Sheet | 3 | of | 6 | Attorney Docket Number | 701586-052823-US |

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| | C10 | Dubik, D., Dembinski, T. C., and Shiu, R. P. Stimulation of c-myc oncogene expression associated with estrogen-induced proliferation of human breast cancer cells. Cancer Res, 47: 6517-6521, 1987. | |
| | C11 | Ferguson, D. R., Kennedy, I., and Burton, T. J. ATP is released from rabbit urinary bladder epithelial cells by hydrostatic pressure changes—a possible sensory mechanism? J Physiol, 505 (Pt 2): 503-511, 1997. | |
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| | C17 | Foster, J. S., Henley, D. C., Bukovsky, A., Seth, P., and Wimalasena, J. Multifaceted regulation of cell cycle progression by estrogen: regulation of Cdk inhibitors and Cdc25A independent of cyclin D1-Cdk4 function. Mol Cell Biol, 21: 794-810, 2001. | |
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| | C20 | Gordon, J. L. Extracellular ATP: effects, sources and fate. Biochem J, 233: 309-319, 1986. | |
| | C21 | Grierson, J. P. and Meldolesi, J. Shear stress-induced [Ca ²⁺] _i transients and oscillations in mouse fibroblasts are mediated by endogenously released ATP: J Biol Chem, 270: 4451-4456, 1995. | |
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| | C26 | Koc, Y., Urbano, A. G., Sweeney, E. B., and McCaffrey, R. Induction of apoptosis by cordycepin in ADA-inhibited TdT-positive leukemia cells. Leukemia, 10: 1019-1024, 1996. | |
| | C27 | Kohno, Y., Sei, Y., Koshiba, M., Kim, H. O., and Jacobson, K. A. Induction of apoptosis in HL-60 human promyelocytic leukemia cells by adenosine A3 receptor agonists. Biochem Biophys Res Commun, 219: 904-910, 1996. | |
| | C28 | Linden, J. Molecular approach to adenosine receptors: receptor-mediated mechanisms of tissue protection. Annu Rev Pharmacol Toxicol, 41: 775-787, 2001. | |
| | C29 | Manni, A., Wright, C., and Buck, H. Growth factor involvement in the multihormonal regulation of MCF-7 breast cancer cell growth in soft agar. Breast Cancer Res Treat, 20: 43-52, 1991. | |

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| | C30 | Neuman, E., Ladha, M. H., Lin, N., Upton, T. M., Miller, S. J., DiRenzo, J., Pestell, R. G., Hinds, P. W., Dowdy, S. F., Brown, M., and Ewen, M. E. Cyclin D1 stimulation of estrogen receptor transcriptional activity independent of cdk4. <i>Mol Cell Biol</i> , 17: 5338-5347, 1997. | |
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| | C32 | Olah, M. E. and Stiles, G. L. Adenosine receptor subtypes: characterization and therapeutic regulation. <i>Annu Rev Pharmacol Toxicol</i> , 35: 581-606, 1995. | |
| | C33 | Park, W. C. and Jordan, V. C. Selective estrogen receptor modulators (SERMS) and their roles in breast cancer prevention. <i>Trends Mol Med</i> , 8: 82-88., 2002. | |
| | C34 | Pianetti, S., Guo, S., Kavanagh, K. T., and Sonenshein, G. E. Green tea polyphenol epigallocatechin-3 gallate inhibits Her-2/neu signaling, proliferation, and transformed phenotype of breast cancer cells. <i>Cancer Res</i> , 62: 652-655., 2002. | |
| | C35 | Podhajcer, O. L., Resnicoff, M., Bover, L., Medrano, E. E., Slavutsky, I., Larripa, I., and Mordoh, J. Effect of estradiol and tamoxifen on the anchorage-independent growth of the subpopulations derived from MCF-7 breast carcinoma cells: cytogenetic analysis of the stem cell subpopulation. <i>Exp Cell Res</i> , 179: 58-64, 1988. | |
| | C36 | Ralevic, V., Milner, P., Kirkpatrick, K. A., and Burnstock, G. Flow-induced release of adenosine 5'-triphosphate from endothelial cells of the rat mesenteric arterial bed. <i>Experientia</i> , 48: 31-34, 1992. | |
| | C37 | Robak, T. The role of nucleoside analogues in the treatment of chronic lymphocytic leukemia-lessons learned from prospective randomized trials. <i>Leuk Lymphoma</i> , 43: 537-548, 2002. | |
| | C38 | Romieu-Mourez, R., Landesman-Bollag, E., Seldin, D. C., Traish, A. M., Mercurio, F., and Sonenshein, G. E. Roles of IKK kinases and protein kinase CK2 in activation of nuclear factor-kappaB in breast cancer. <i>Cancer Res</i> , 61: 3810-3818., 2001. | |
| | C39 | Schrier, S. M., van Tilburg, E. W., van der Meulen, H., Ijzerman, A. P., Mulder, G. J., and Nagelkerke, J. F. Extracellular adenosine-induced apoptosis in mouse neuroblastoma cells: studies on involvement of adenosine receptors and adenosine uptake. <i>Biochem Pharmacol</i> , 61: 417-425, 2001. | |

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| C40 | Sun, S. and Ravid, K. Role of a serine/threonine kinase, Mst1, in megakaryocyte differentiation. J Cell Biochem, 76: 44-60., 1999. |
| C41 | Tamoxifen for early breast cancer: an overview of the randomised trials. Early Breast Cancer Trialists' Collaborative Group. Lancet, 351: 1451-1467., 1998. |
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| C43 | Tey, H. B., Tan, C. H., and Khoo, H. E. Modulation of DNA synthesis via adenosine receptors in human epidermoid carcinoma (A431) cells. Biofactors, 4: 161-165, 1994. |
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| C45 | Wang, Z., Zhang, Y., Lu, J., Sun, S., and Ravid, K. Mpl ligand enhances the transcription of the cyclin D3 gene: a potential role for Sp1 transcription factor. Blood, 93: 4208-4221., 1999. |
| C46 | Watts, C. K., Sweeney, K. J., Warlters, A., Musgrove, E. A., and Sutherland, R. L. Antiestrogen regulation of cell cycle progression and cyclin D1 gene expression in MCF-7 human breast cancer cells. Breast Cancer Res Treat, 31: 95-105, 1994. |
| C47 | Williams, W., Craver, R. D., Correa, H., Velez, M., and Gardner, R. V. Use of 2-chlorodeoxyadenosine to treat infantile myofibromatosis. J Pediatr Hematol Oncol, 24: 59-63, 2002. |
| C48 | Yao, Y., Sei, Y., Abbracchio, M. P., Jiang, J. L., Kim, Y. C., and Jacobson, K. A. Adenosine A3 receptor agonists protect HL-60 and U-937 cells from apoptosis induced by A3 antagonists. Biochem Biophys Res Commun, 232: 317-322, 1997. |

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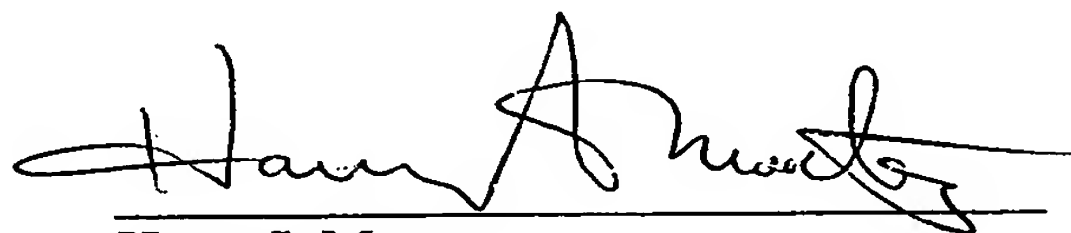
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